

What is claimed is:

Subt
a/

1. A free-acid form of hyaluronic acid, made by the method comprising the steps of:

a) dissolving an alkali-metal salt of hyaluronic acid in water to form a solution,

b) dispersing in said solution an acid capable of producing a pH of 2.2 or lower at concentrations in water at 25° C of 0.01 Normal to 1 Normal,

c) enclosing the dispersion formed in step (b) within a semi-permeable membrane having a molecular weight cut-off at least large enough to pass said acid,

d) dialyzing the dispersion in water while the dispersion is so enclosed, and

e) harvesting free hyaluronic acid from within the semi-permeable membrane.

2. The product of Claim 1, wherein the membrane is chosen to be non-ionic.

3. The product of Claim 1, wherein the acid added in step (b) is an acid selected from the group consisting of hydrochloric acid, sulfuric acid, nitric acid, orthophosphoric acid, and oxalic acid.

4. The product of Claim 1, wherein the semi-permeable membrane is made from a material selected from the group consisting of regenerated cellulose and cellulose esters.

5. The product of Claim 1, wherein the molecular weight cut-off of the semi-permeable membrane is at least twice as great as that needed to pass the acid added in step (b).

6. The product of Claim 1, wherein the ratio of volume of the water

used to dialyze in step (d), to the volume of the hyaluronate solution, is 5:1 or less.

7. The product of Claim 1, wherein the steps are performed at a temperature in the range of about 4-30° C.

8. The product of Claim 1, wherein the dialyzing step is performed until water surrounding the membrane has a predetermined pH.

9. A free-acid form of a polysaccharide, made by the method comprising the steps of:

- a) dissolving a salt of a polysaccharide in water to form a solution,
- b) dispersing an acid in said solution,
- c) enclosing the dispersion formed in step (b) within a semi-permeable membrane,
- d) dialyzing the dispersion in water while the dispersion is so enclosed, and
- e) harvesting a free acid form of the polysaccharide from within the semi-permeable membrane.

10. The product of Claim 9, wherein the membrane is selected to be non-ionic.

11. The product of Claim 9, wherein the polysaccharide salt is sodium hyaluronate.

12. The product of Claim 9, wherein the acid added in step (b) is an acid selected from the group consisting of hydrochloric acid, sulfuric acid, nitric acid, orthophosphoric acid, and oxalic acid.

13. The product of Claim 9, wherein the semi-permeable membrane has a molecular weight cut-off large enough to pass the acid added in step (b).

14. The product of Claim 13, wherein the semi-permeable membrane is made from a material selected from the group consisting of regenerated cellulose and cellulose esters.

15. The product of Claim 13, wherein the molecular weight cut-off of the semi-permeable membrane is at least twice as great as that needed to pass the acid added in step (b).

16. The product of Claim 9, wherein the ratio of volume of the water used to dialyze in step (d), to the volume of the solution of step (b), is 5:1 or less.

17. The product of Claim 9, wherein the steps are performed at a temperature in the range of about 4-30° C.

18. The product of Claim 9, wherein the dialyzing step is performed until water surrounding the membrane has a predetermined pH.

19. The product of Claim 9, wherein the polysaccharide is selected from the group consisting of chondroitin sulfate, heparin, and carboxymethyl cellulose.

20. A free-acid form of hyaluronic acid, made by the method comprising the steps of:

a) preparing a solution of sodium hyaluronate in distilled water,
b) mixing into said solution an acid capable of producing a pH of 2.2 or lower at concentrations in water at 25° C in the range of 0.01 Normal to 1 Normal, to produce a mixture,

c) enclosing said mixture in a dialysis bag having a molecular weight cut-off large enough to pass the acid added in step (b),

d) placing the bag in de-ionized water,

e) periodically replacing the de-ionized water with fresh de-ionized water, until the pH of the de-ionized water exceeds 5.0, and

f) ~~harvesting free hyaluronic acid from within the bag.~~

21. The product of Claim 20, wherein the dialysis bag comprises a non-ionic membrane.

22. The product of Claim 20, wherein the acid added in step (b) is hydrochloric acid.

23. The product of Claim 20, wherein the molecular weight cut-off of the bag is 3500.

2025-07-10 10:10:10